SYNTHESIS OF COMPOUNDS RELATED TO 2,6-DIALKYLPHENYLHYDRAZINES

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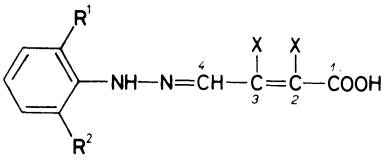
2,6-Dialkylphenylhydrazines were the starting materials for the synthesis of 2,3-dichloro- and 2,3-dibromo-4-(2′,6′-dialkylphenylhydrazino)butenoic acids *Ia—If* and 3-(2′,6′-dialkylphenylhydrazinocarbonyl)propionic acids *IIIa—IIIc*. Compounds *IIIa—IIIc* cyclized to give 2-(2,6-dialkylphenyl)-2,3-dihydropyridazine-3,6-diones *Va—Vc*. Chloro-, bromo- and dichloromaleic anhydride reacted with the starting hydrazines to furnish N-(2′,6′-dialkylphenylamino)maleimides *IVa—IVi*. N-((2,2,2-Trichloro-1-formylamino)ethyl)-2,6-dialkylphenylhydrazines *VIa—VIc*, obtained from the starting hydrazines and N-(1,2,2,2-tetrachloroethyl)formamide together with other products were tested as pesticides.

Several patents[1-8] appearing in the last 15 years utilized 2,6-dialkylphenylhydrazines[9,10] and especially 2,6-dimethylphenylhydrazine for the synthesis of fungicidally active substances. The latter was also employed[11] for an interesting synthesis of 3-amino-1,3-thiazolidinediones, hypnotically active thiazolines[12,13] and derivatives of 5-pyrazolecarboxylic acid having a sedative, hypnotic and myorelaxation effects. 2,6-Dimethylphenylhydrazonium chloride was also reported[14] to react with phenyl ketones to yield substituted pyrazoles utilizable as scintillators and fluorescent bleachers avoiding yellowing of synthetic fibres.

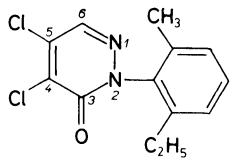
2,6-Dialkyphenylhydrazines also served for preparation of substituted 1,2,4-triazole derivatives[15], indolylformazanes, indolylazetidinones and tetrazolium salts[16]. 2,6-Dialkylphenylhydrazones undergo new rearrangements[10,17-19]; the action of weak oxidation reagents on 2,6-dimethylphenylhydrazine and its derivatives was investigated[20-22] as well.

This paper describes reactions of 2,3-dichloro-4-oxobutenoic acid with 2,6-dialkylphenylhydrazines. Results of this reaction depended on reaction conditions. Thus, in an aqueous medium the above-mentioned acid and its bromo analogue reacted with 2,6-dialkyphenylhydrazinium chlorides to deposit hydrazones *Ia—If* (Table I). This acid reacted analogously with phenylhydrazinium chloride[23]. 2-Ethyl-6-methylphenylhydrazinium chloride on treatment with 4-oxo-2,3-dichloro-2-butenoic acid

in acid (HCl) medium afforded substituted 2,3-dihydropyridazine-3-one (*II*). Dialkylphenylhydrazines and maleic anhydride, chloro-, bromo- and dichloromaleic anhydride furnished various products. In benzene, maleic anhydride reacted with the starting 2,6-dialkylphenylhydrazines to give 3-(2′,6′-dialkylhydrazinocarbonyl)-propenoic acids *IIIa–IIIc*, which cyclized in acetic anhydride in the presence of sodium acetate under formation of substituted 2,3-dihydropyridazine-3,6-diones



	R^1	R^2	X
Ia	CH_3	CH_3	Cl
Ib	CH_3	C_2H_5	Cl
Ic	C_2H_5	C_2H_5	Cl
Id	CH_3	CH_3	Br
Ie	CH_3	C_2H_5	Br
If	C_2H_5	C_2H_5	Br



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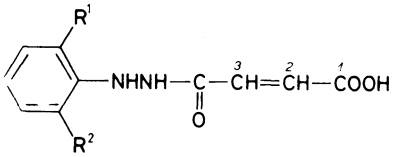
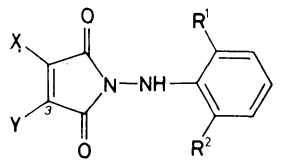
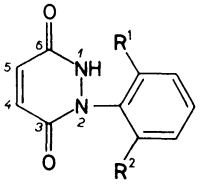


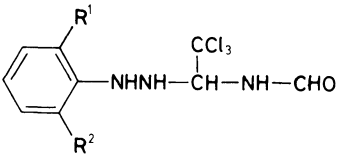
IIIa, $R^1 = R^2 = CH_3$
IIIb, $R^1 = CH_3$; $R^2 = C_2H_5$
IIIc, $R^1 = R^2 = C_2H_5$



	R^1	R^2	X	Y
IVa	CH_3	CH_3	Br	H
IVb	CH_3	C_2H_5	Br	H
IVc	C_2H_5	C_2H_5	Br	H
IVd	CH_3	CH_3	Cl	Cl
IVe	CH_3	C_2H_5	Cl	Cl
IVf	C_2H_5	C_2H_5	Cl	Cl



Va, $R^1 = R^2 = CH_3$
Vb, $R^1 = CH_3$; $R^2 = C_2H_5$
Vc, $R^1 = R^2 = C_2H_5$



VIa, $R^1 = R^2 = CH_3$
VIb, $R^1 = CH_3$; $R^2 = C_2H_5$
VIc, $R^1 = R^2 = C_2H_5$

TABLE I

Characteristic data of compounds *I*–*VI*

Compound	Formula (M.w.)	M.p., °C Yield, %	Calculated/Found			
			% C	% C	% H	% Hal
Ia	$C_{12}H_{12}Cl_2N_2O_2$ (287·1)	142–144 72	50·20 50·65	4·21 4·21	9·75 9·75	24·69 24·22
Ib	$C_{13}H_{14}Cl_2N_2O_2$ (301·1)	126–127 76	51·85 51·62	4·68 4·32	9·30 9·60	23·54 23·16
Ic	$C_{14}H_{16}Cl_2N_2O_2$ (315·2)	126–128 74	53·35 53·20	5·11 4·92	8·89 8·46	22·50 22·69
Id	$C_{12}H_{12}Br_2N_2O_2$ (376·0)	107–109 77	38·33 38·32	3·21 3·42	7·45 7·15	42·50 41·98
Ie	$C_{13}H_{14}Br_2N_2O_2$ (390·1)	84–90 80	40·03 40·16	3·61 3·72	7·18 7·14	40·97 40·86
If	$C_{14}H_{16}Br_2N_2O_2$ (404·1)	118–119 76	41·61 41·19	3·99 3·96	6·94 6·89	39·55 39·12
IIIa	$C_{12}H_{14}N_2O_3$ (234·2)	145–150 68	61·54 61·26	6·02 5·98	11·96 12·16	
IIIb	$C_{13}H_{16}N_2O_3$ (248·2)	122–126 72	62·91 62·76	6·49 6·56	11·28 11·40	
IIIc	$C_{14}H_{18}N_2O_3$ (262·3)	133–135 76	64·11 64·18	6·94 6·56	10·68 10·28	
IVa	$C_{12}H_{11}BrN_2O_2$ (295·1)	138–139 69	48·84 49·22	3·75 3·79	9·49 9·59	27·01 26·90
IVb	$C_{13}H_{13}BrN_2O_2$ (309·1)	66–69 68	50·52 50·16	4·21 4·01	9·06 9·17	25·85 25·60
IVc	$C_{14}H_{15}BrN_2O_2$ (323·2)	79–81 66	52·03 53·03	4·68 4·46	8·67 8·42	24·72 23·98
IVd	$C_{12}H_{10}Cl_2N_2O_2$ (285·1)	134–135 90	50·55 49·90	3·53 3·57	9·82 9·77	24·87 24·90
IVe	$C_{13}H_{12}Cl_2N_2O_2$ (299·1)	112–113 92	52·19 52·15	4·04 3·80	9·36 9·30	23·70 23·60
IVf	$C_{14}H_{14}Cl_2N_2O_2$ (313·2)	115 89	53·69 53·50	4·50 4·40	8·94 8·92	22·69 22·56
Va	$C_{12}H_{12}N_2O_2$ (216·2)	71 82	66·65 67·19	5·59 5·59	12·95 13·31	
Vb	$C_{13}H_{14}N_2O_2$ (230·2)	57–59 80	67·81 67·60	6·12 6·19	12·16 12·42	

TABLE I
(*Continued*)

Compound	Formula (M.w.)	M.p., °C Yield, %	Calculated/Found			
			% C	% H	% N	% H
Vc	$C_{14}H_{16}N_2O_2$	70–72	68·83	6·60	11·46	
	(244·3)	81	68·43	6·80	11·56	
VIa	$C_{11}H_{14}N_3Cl_3O$	127–130	40·45	4·32	12·86	32·56
	(326·6)	73	40·12	4·10	12·72	33·10
VIb	$C_{12}H_{16}N_3Cl_3O$	124–126	42·31	4·73	12·34	31·22
	(340·6)	77	43·02	4·76	12·56	31·28
VIc	$C_{13}H_{18}N_3Cl_3O$	129–131	44·02	5·11	11·85	29·99
	(354·6)	89	44·64	5·39	12·18	29·63

Va – Vc. N-(2′,6′-Dialkylamino)bromomaleimides *IVa – IVc* and their dichloro analogues *IVd – IVf* were obtained by reacting 2,6-dialkylphenylhydrazines with the corresponding halogenated maleic anhydrides in benzene.

As known, N-(2,2,2-trichloro-1-formylamino)ethyl residue is embodied in commercial fungicides (Triforine[24] and Trimorphamide[25]); compounds *VIa – VIc*, characterized by this feature were synthesized from N-(1,2,2,2-trichloroethyl)formamide and 2,6-dialkylphenylhydrazines.

The structure of the synthesized compounds was verified by ^{1}H NMR spectral data (Tables II – V). The infrared spectra were indicative of carbonyl absorption bands appearing at 1 680 cm^{-1} (*Ia – If*), 1 750 cm^{-1} (*IIIa – IIIc*), 1 738 cm^{-1} (*IVa – IVc*) and 1 720 – 1 725 cm^{-1} (*Va – Vc*). These products were tested as potential pesticides by standard methods for fungicide[26] and herbicide[27] activities, but none of them achieved properties of the references.

EXPERIMENTAL

The ^{1}H NMR spectra were measured at 80 MHz in deuteroacetone, tetramethylsilane being the internal reference. The infrared spectra were recorded on a Specord 71 IR spectrometer in chloroform.

2,6-Dialkylphenylhydrazinium chlorides were prepared according to literature[9,10]; 2,6-dialkylphenylhydrazines were freed from their crystalline salts with sodium hydroxide.

2,3-Dichloro-4-(2′,6′-dimethylphenylhydrazono)butenoic Acid (*Ia*)

2,6-Dimethylphenylhydrazinium chloride (1·7 g, 10 mmol) in water (50 ml) was added to a stirred solution of 4-oxo-2,3-dichloro-2-butenoic acid (1·7 g, 10 mmol) in water (350 ml) at 20°C. After

TABLE II

^{1}H NMR data (δ, ppm) for compounds *I* and *III*

Compound[a]	H-2[b]	H-3	H-4	H-arom	R^1	R^2
Ia	—	—	8·57 s	7·08 bs	2·35 s	2·35 s
Ib	—	—	8·46 s	7·06 bs	2·27 s	2·70 s 1·15 t
Ic	—	—	8·50 s	7·12 bs	2·70 q 1·16 t	2·70 q 1·16 t
Id	—	—	8·20 s	7·00 bs	2·30 s	2·30 s
Ie	—	—	8·21 s	7·06 bs	2·30 s	2·70 q 1·15 t
If	—	—	8·20 s	7·09 bs	2·67 q 1·12 t	2·67 q 1·12 t
IIIa	6·57 d	6·30 d	—	6·97 bs	2·37 s	2·37 s
IIIb	6·55 d	6·28 d	—	7·02 bs	2·37 s	2·80 q 1·20 t
IIIc	6·55 d	6·28 d	—	7·05 bs	2·80 q 1·20 t	2·80 q 1·20 t

[a] For *Ia*—*If*: COOH and NH protons showed broad signals at ppm 9·25—9·68 and 8·62—9·68, for *IIIa*—*IIIc*: 10·00 bs, 1 H (COOH); 7·00 bs, 1 H (NH). [b] $J(2, 3) = 13·0$ Hz.

TABLE III

^{1}H NMR data (δ, ppm) for compounds *IV*

Compound	H-3	H-arom	R^1	R^2	NH
IVa	7·19 s	6·90 bs	2·27 s	2·27 s	6·57 bs
IVb	7·16 s	6·93 bs	2·25 s	2·73 q 1·12 t	6·61 bs
IVc	7·20 s	7·00 bs	2·62 q 1·13 t	2·62 q 1·13 t	6·60 bs
IVd	—	6·95 bs	2·30 s	2·30 s	6·62 bs
IVe	—	6·96 bs	2·30 s	2·62 q 1·15 t	6·70 bs
IVf	—	7·02 bs	2·77 q 1·15 t	2·77 q 1·15 t	6·72 bs

3 h-stirring at this temperature the separated precipitate was filtered off, washed with water ether and dried at 40°C.

Compounds *Ib* and *Ic* were prepared in the same way and compounds *Id*—*If* by employing 4-oxo-2,3-dibromo-2-butenoic acid.

2-(2'-Ethyl-6'-methylphenyl)-4,5-dichloro-2,3-dihydropyridazin-3-one (*II*)

Concentrated hydrochloric acid (10 ml) and 4-oxo-2,3-dichloro-2-butenoic acid (3·4 g, 20 mmol) were added to a solution of 2-ethyl-6-methylphenylhydrazinium chloride (5·6 g, 20 mmol) with stirring, which continued at 90°C for 2 h. The mixture was cooled and the crystalline product was filtered off; yield of *II* 5·3 g (94%), m.p. 121·5°C (toluene). For $C_{13}H_{12}Cl_2N_2O$ (283·3) calculated: 55·11% C, 4·27% H, 25·03% Cl, 9·94% N; found: 54·98% C, 4·28% H, 24·96% Cl, 9·90% N. ^{1}H NMR ($CDCl_3$): 7·92 s, 1 H (H-6); 7·23 m, 3 H (H-arom); 2·05 s, 3 H (CH_3); 2·36 q, 2 H (CH_2); 1·11 t, 3 H (CH_3).

TABLE IV

^{1}H NMR data (δ, ppm) for compounds *V*

Compound	H-4[a]	H-5	H-arom	R^1	R^2	NH
Va	6·41 d	7·50 d	7·02 bs	2·35 s	2·35 s	8·68 bs
Vb	6·32 d	7·49 d	7·04 bs	2·31 s	2·63 q 1·16 t	8·53 bs
Vc	6·32 d	7·48 d	7·09 bs	2·73 q 1·15 t	2·73 q 1·15 t	8·53 bs

[a] $J(4, 5) = 5·5$ Hz.

TABLE V

^{1}H NMR data (δ, ppm) for compounds *VI*

Compound	CH=O	CH	H-arom	R^1	R^2	NH[a]	NH[b]
VIa	8·47 s	5·50 t	6·87 bs	2·31 s	2·31 s	8·00 bs	4·78 bs
VIb	8·47 s	5·56 t	6·91 bs	2·33 s	2·77 q 1·13 t	8·00 bs	4·80 bs
VIc	8·50 s	5·53 t	6·91 bs	2·82 q 1·17 t	2·82 q 1·17 t	8·06 bs	4·80 bs

[a] Signal 1 H; [b] signal 2 H.

3-(2′,6′-Dimethylphenylhydrazinocarbonyl)propenoic Acid (*IIIa*)

2,6-Dimethylphenylhydrazine (2·7 g, 20 mmol) in benzene (10 ml) was added to maleic anhydride (2·0 g, 20 mmol) dissolved in benzene (20 ml). The mixture was refluxed for 1 h, cooled and the separated precipitate was filtered off. Compounds *IIIb* and *IIIc* were prepared by the same procedure.

N-(2′,6′-Dimethylphenylamino)bromomaleimide (*IVa*)

2,6-Dimethylphenylhydrazine (2·7 g, 20 mmol) in benzene (10 ml) was added to a solution of bromomaleic anhydride (3·5 g, 20 mmol) in benzene (40 ml). The mixture was refluxed, the reaction water was removed, the solvent was distilled off under reduced pressure and the residue was crystallized from ethanol. Compounds *IVb* and *IVc* were prepared analogously.

Compounds *IVd*—*IVf* were synthesized from dichloromaleic anhydride in the same way.

2-(2′,6′-Dimethylphenyl)-2,3-dihydropyridazine-3,6-dione (*Va*)

A mixture consisting of *IIIa* (4·6 g, 20 mmol), anhydrous sodium acetate (0·8 g) and acetic anhydride (20 ml) was stirred at 60°C for 30 min, poured on crushed ice, the precipitate was filtered off and crystallized from ethanol. Compounds *Vb* and *Ve* were synthesized by the same procedure.

N-[(2,2,2-Trichloro-1-formylamino)ethyl]-2,6-dimethylphenylhydrazine (*VIa*)

N-(1,2,2,2-tetrachloroethyl)formamide (3·16 g, 15 mmol) in benzene (20 ml) was added to a suspension of 2,6-dimethylphenylhydrazine (2·04 g, 15 mmol) and sodium carbonate (2·1 g, 20 mmol) in benzene (15 ml) with stirring at room temperature. After 2 h the mixture was filtered and the solution was concentrated to a half of its volume. The precipitate was filtered off and crystallized from tetrachloromethane. Compounds *VIb* and *VIc* were prepared by an analogous procedure.

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